
PRESS RELEASEFOR IMMEDIATE RELEASE

Defusing a ‘ticking time bomb’: Groundbreaking research offers early clues to stomach cancer development

Researchers uncover genetic factors allowing for the early prediction of intestinal metaplasia patients who may have higher risks of developing stomach cancer, enabling early detection, diagnosis and targeted prevention

SINGAPORE, 11 December 2023 – In a breakthrough study published in the highly respected journal *Cancer Cell*¹, researchers have decoded critical genetic factors in intestinal metaplasia patients, shedding light on early signs and prevention strategies for stomach cancer – often a “ticking time bomb” as patients experience no or only mild symptoms in the early stages.

Intestinal metaplasia, which is a change in the cells of the mucous membrane lining the stomach that often stems from chronic gastritis and manifests with symptoms akin to acid reflux, is also a sinister link to stomach cancer. Individuals afflicted with intestinal metaplasia cells face a sixfold increased risk of succumbing to this lethal cancer.

In Singapore alone, stomach cancer ranks as the fourth leading cause of cancer deaths in men and the fifth among women, claiming 300 to 500 lives annually, largely due to late detection. Two thirds of stomach cancer patients are only diagnosed at an advanced stage.

Unveiling early indicators through collaborative breakthrough research

The longitudinal study, which represents the world’s largest genomic survey of patients with intestinal metaplasia, examines more than 1,100 tissue samples using powerful technologies such as single-cell RNA sequencing and spatial transcriptomics². Based on this extensive survey, researchers identified 26 ‘driver genes’ that play a pivotal role in the transition to stomach cancer. This landmark finding provides a glimpse into the mechanisms governing the transformation and offers a critical window for early detection and targeted prevention.

“Advances in DNA sequencing have made it possible for us to uncover diverse cell populations within these stomach changes, hinting at their potential transformation into cancerous cells influenced by various factors. It’s akin to understanding the ticking mechanism of a time bomb,” explained Dr Huang Kie Kyon, co-first author and Senior Research Fellow with the Cancer & Stem Cell Biology Programme at Duke-NUS Medical School (Duke-NUS).

¹ Spatiotemporal genomic profiling of intestinal metaplasia reveals clonal dynamics of gastric cancer progression. <https://pubmed.ncbi.nlm.nih.gov/37890493/>

² Single-cell RNA sequencing (scRNA-seq) is a powerful technology that allows scientists to study individual cells’ genetic material (RNA) one cell at a time. Spatial transcriptomics is another technique used to study gene expression in tissues but with an added dimension of spatial information. It allows scientists to see where specific genes are being expressed within tissues or organs, providing insight into the organisation and communication between cells in their actual location within the tissue.

Professor Patrick Tan, Senior Vice-Dean for Research at Duke-NUS and a professor with the School's Cancer & Stem Cell Biology Programme said: "The comprehensive dataset we've assembled provides unprecedented insights into the progression of cell changes in the stomach to cancer. By using both clinical information and genetic data from advanced molecular technologies, we can better predict which stomach conditions might turn into stomach cancer compared to using only clinical information. This can help in the development of new and more precise ways to prevent and stop stomach cancer." Prof Tan is also a member of the Genome Institute of Singapore, Cancer Science Institute of Singapore, and Precision Health Research Singapore (PRECISE).

The multi-institutional effort by researchers from Duke-NUS, National University Hospital (NUH), National University of Singapore's Yong Loo Lin School of Medicine (NUS Medicine) and Seoul National University Hospital reflects the strengths of Singapore's multi-institutional cancer research ecosystem and its strong links with global partners. This study was supported by the Singapore Gastric Cancer Consortium (SGCC), a national translational research group comprising clinicians and scientists working in stomach cancer research from academic medical centres, universities, hospitals and research institutes across Singapore. The published work is derived from the prospective Gastric Cancer Epidemiology Programme cohort.

The study offers clues into whether intestinal metaplasia cells directly transform into stomach cancer. It was revealed that a subpopulation of intestinal stem-like cells in patients with intestinal metaplasia closely resembles early stomach cancer cells, pointing to a possible early origin and potential of its malignant future. This discovery highlights the importance of screening for intestinal metaplasia in managing stomach cancer risk.

Co-senior author Professor Jimmy So, Head & Senior Consultant, Division of General Surgery (Upper Gastrointestinal Surgery), NUH commented on the clinical implications: "This molecular roadmap of disease progression from intestinal metaplasia offers many translational opportunities. We can now explore more targeted surveillance for patients at highest risk, as well as anti-inflammatory or antibiotic agents to intercept premalignant clones before they evolve into cancer, potentially leading to improved patient outcomes through early detection." He is also a professor at the Department of Surgery, NUS Medicine.

More efficient and targeted preventive measures for populations

At the population level, the findings hold promise for refining screening strategies and allocating resources more effectively to intercept the development of gastric cancer in high-risk individuals, ultimately contributing to more efficient and targeted preventive measures. This is especially relevant in countries such as Singapore, where the incidence of stomach cancer is moderate compared to Japan and South Korea where stomach cancer incidence is high enough to warrant mass screening.

"Encouragingly, our results revealed that combining genomic data with clinical check-ups can make predictions about stomach cancer more accurate. This means we might use genetic tests, including simple and inexpensive blood tests, to identify people who are at a very high risk of getting stomach cancer. With this approach, we can divide people into groups based on their risk using either regular check-ups or these affordable blood tests. This helps to save resources by making sure those at the highest risk get the right tests and care they need," added Professor Yeoh Khay Guan, Lead Principal Investigator of the Singapore Gastric Cancer Consortium and Senior Consultant in the Division of Gastroenterology & Hepatology, National University Hospital. Prof

Yeoh is also the Kishore Mahbubani Professor in Medicine and Health Policy, Department of Medicine, NUS Medicine.

Senior author Associate Professor Chung Hyunsoo from Seoul National University Hospital stressed the clinical ramifications: “This breakthrough may refine screening protocols, enabling early interventions for high-risk patients, while sparing others unnecessary procedures.”

The research was funded by the prestigious Open Fund-Large Collaborative Grant that is supported by the National Research Foundation, Singapore and administered by the Singapore Ministry of Health’s National Medical Research Council. The team also received support from Singapore’s Ministry of Education, Cancer Science Institute of Singapore under the National University of Singapore and the Francis Crick Institute. In addition, the project could not have been made possible without the contributions of researchers from Tan Tock Seng Hospital, Singapore General Hospital, Changi General Hospital, Nihon University School of Medicine, Yonsei University Wonju College of Medicine and The Chinese University of Hong Kong.

Reference: Huang KK, Ma H, Chong RHH, et al. *Spatiotemporal Genomic Profiling of Intestinal Metaplasia Reveals Clonal Dynamics of Gastric Cancer Progression. Cancer Cell.* 2023;doi:[10.1016/j.ccell.2023.10.004](https://doi.org/10.1016/j.ccell.2023.10.004).

About Duke-NUS Medical School

Duke-NUS is Singapore's flagship graduate entry medical school, established in 2005 with a strategic, government-led partnership between two world-class institutions: Duke University School of Medicine and the National University of Singapore (NUS). Through an innovative curriculum, students at Duke-NUS are nurtured to become multi-faceted 'Clinicians Plus' poised to steer the healthcare and biomedical ecosystem in Singapore and beyond. A leader in ground-breaking research and translational innovation, Duke-NUS has gained international renown through its five signature research programmes and 10 centres. The enduring impact of its discoveries is amplified by its successful Academic Medicine partnership with Singapore Health Services (SingHealth), Singapore's largest healthcare group. This strategic alliance has spawned 15 Academic Clinical Programmes, which harness multi-disciplinary research and education to transform medicine and improve lives.

For more information, please visit www.duke-nus.edu.sg

About National University Hospital

The National University Hospital (NUH) is Singapore's leading university hospital. While the hospital at Kent Ridge first received its patients on 24 June 1985, our legacy started from 1905, the date of the founding of what is today the NUS Yong Loo Lin School of Medicine. NUH is the principal teaching hospital of the medical school.

Our unique identity as a university hospital is a key attraction for healthcare professionals who aspire to do more than practise tertiary medical care. We offer an environment where research and teaching are an integral part of medicine, and continue to shape medicine and transform care for the community we care for.

We are an academic medical centre with over 1,200 beds, serving more than one million patients a year with over 50 medical, surgical and dental specialties. NUH is the only public and not-for-profit hospital in Singapore to provide trusted care for adults, women and children under one roof, including the only paediatric kidney and liver transplant programme in the country.

The NUH is a key member of the National University Health System (NUHS), one of three public healthcare clusters in Singapore.

About the NUS Yong Loo Lin School of Medicine

The NUS Yong Loo Lin School of Medicine is Singapore's first and largest medical school. Our enduring mission centres on nurturing highly competent, values-driven and inspired healthcare professionals to transform the practice of medicine and improve health around the world.

Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,000 graduates have passed through our doors.

In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is one of Asia's leading medical schools and ranks among the best in the world (Times Higher Education World University Rankings 2023 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2023).

For more information about NUS Medicine, please visit <https://medicine.nus.edu.sg/>.

About Seoul National University Hospital

Seoul National University Hospital (SNUH), Korea's central national hospital, has been the pioneer of western medicine in Korea and has cared for the health of Korean citizens. With 3,836 beds, SNUH provides reliable quality medical service to over 10,000 outpatients and about 3,500 inpatients every day. SNUH consists of the Main Hospital, Children's Hospital, Cancer Hospital, Biomedical Research Institute, SNUH Center for Medical Innovation, SNU Bundang Hospital, SMG-SNUH Boramae Medical Center, SNUH Healthcare System Gangnam Center, National Traffic Injury Rehabilitation Hospital, and Sheikh Khalifa Specialty Hospital (SKSH) with over 10,000 staff members.

Furthermore, SNUH is a leading teaching hospital training over 1,200 doctors, who are to become specialists, and a top-notch research-centered hospital publishing over 2,400 articles in world's prominent SCI journals every year. For clinical trials in oncology, SNUH conducted over 600 studies in the past five years.

For more information, please visit www.snuh.org

For media enquiries, please contact:

Alice Chia
Communications
Duke-NUS Medical School
Email: alice.chia@duke-nus.edu.sg

Hoi Wan Theng
Group Communications
National University Health System
Email: wan_theng_hoi@nuhs.edu.sg

Youngjoo Park
Press Relations
Seoul National University Hospital
Email: yjp@snuh.org

Annex A: Chinese Translations

Duke-NUS Medical School (Official name, for use on first reference)	杜克 - 新加坡国立大学医学院
Duke-NUS (abbreviated form)	杜克 - 国大医学院
National University Hospital (NUH)	国立大学医院 (国大医院)
NUS Yong Loo Lin School of Medicine (NUS Medicine)	新加坡国立大学杨潞龄医学院 (国大杨潞龄医学院)
Professor Patrick Tan Senior Vice-Dean for Research Duke-NUS Medical School	陈文炜 教授 研究高级副院长 杜克 - 新加坡国立大学医学院
Professor Yeoh Khay Guan Senior Consultant Division of Gastroenterology & Hepatology Department of Medicine National University Hospital	杨啟源教授 高级顾问医生 肠胃与肝脏科 国立大学医院
Kishore Mahbubani Professor in Medicine and Health Policy Department of Medicine NUS Yong Loo Lin School of Medicine	Kishore Mahbubani 医学及医疗保健政策教授 新加坡国立大学杨潞龄医学院内科系
Professor Jimmy So Head and Senior Consultant Division of General Surgery (Upper Gastrointestinal Surgery) Department of Surgery National University Hospital	苏博欣教授 上肠胃外科主任兼高级顾问医生 国立大学医院
Department of Surgery, NUS Yong Loo Lin School of Medicine	杨潞龄医学院外科系 新加坡国立大学
Dr Huang Kie Kyon Senior Research Fellow Cancer & Stem Cell Biology Programme Duke-NUS Medical School	范其建 博士 高级研究员 癌症与干细胞生物学研究 杜克 - 新加坡国立大学医学院